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PATENT
454313-2250.1

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants	:	Jean-Christophe AUDONNET *et al.*
Serial No.	:	10/085,519
Filing Date	:	February 28, 2002
For	:	POLYNUCLEOTIDE VACCINE FORMULA IN PARTICULAR AGAINST BOVINE RESPIRATORY PATHOLOGY
Examiner	:	Z. Lucas
Art Unit	:	1648

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DECLARATION UNDER 37 C.F.R. 1.132

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

I, Dr. Jean-Christophe Audonnet, declare and state that:

1. I make this declaration in connection with U.S. application Serial No. 10/085,519. I am a co-inventor of this application and am familiar with its prosecution history, particularly the Office Action mailed on June 3, 2003, as it pertains to the rejection under 35 U.S.C. §103(a) of claims 12-15 and 18 as allegedly being unpatentable over Klippmark *et al.* in view of Suzu *et al.* and in further view of Felgner *et al.* and Crowe *et al.*, considered in light of the teachings of Wathen *et al.* and Babiuk *et al.*

2. I am a citizen of France. As indicated on my attached *Curriculum vitiae*, I received a veterinary degree from Ecole Nationale Vétérinaire d'Alfort in 1980, a master's

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degree in molecular biology and genetics from University Montpellier in 1984, and a doctorate in molecular biology from Lyon University in 1989. I have also received a Certificate of Compared and Animal Immunology, a Certificate of Immunology and a degree in general virology. I have been employed by Merial, the assignee of this application, since September, 1997, and have served as Director of Molecular Biology and Immunology since May, 2001. From June, 1993 to September, 1997, I was employed as Head of the Molecular Biology and Genetic Recombination Units by Merial's predecessor company, Rhône Mérieux Lyon. In view of my education and experience, I consider myself to be an expert in the field to which this application pertains.

3. The following experiments were performed by under my supervision or control, and in the ordinary course of business.

Aim: To evaluate the immune response in cattle after administration of a mixture of two plasmids, one expressing BPIV-3 HN gene, and one expressing BPIV-3 F gene.

Methods: Cattle were given two intradermal injections, 28 days apart, of an immunogenic composition comprising 600 μg of each plasmid. On day 56, animals were challenged with 10^8-10^9 $TCID_{50}$ BPIV-3, and neutralizing titers, clinical scores and viral excretion were measured. For comparison, a second group of animals was immunized according to the same schedule with a commercial vaccine containing live attenuated virus. (n = 12 animals per group)

Results: As is shown in Table 1 and Figure 1, the clinical scores for animals that received the claimed composition were similar to those that received a commercially available live attenuated vaccine, and lower than a control group of cattle. Table 2 and Figure 2 demonstrate that the percentage of animals with detectable viral excretion was markedly decreased over the control group at 5 days post-challenge for both the claimed composition and the commercially available vaccine. Finally, Table 3 shows that bovines receiving the claimed composition had a significantly higher neutralizing antibody titer than control animals, and more than animals receiving the commercial vaccine. (Antibody titers are expressed as $\log_2$ units.)

Table 1.

Day	Clinical scores		
	PIV3 DNA vaccine	Commercial vaccine	Control
1	0.08	0	0.1
2	0.42	0.91	0.4
3	0.75	1	0.8
4	0.83	1	0.7
5	0.83	1	1
6	1	1	1
7	0.83	0.91	1.3
8	1.08	1.18	1.6
9	1.33	1.09	1.4
10	1.5	1.09	1.1
11	1.5	1.18	1.7
12	1.42	1.36	1.8
13	1.33	1	1.7
14	0.92	0.7	2
15	1	0.8	1.9

Figure 1.

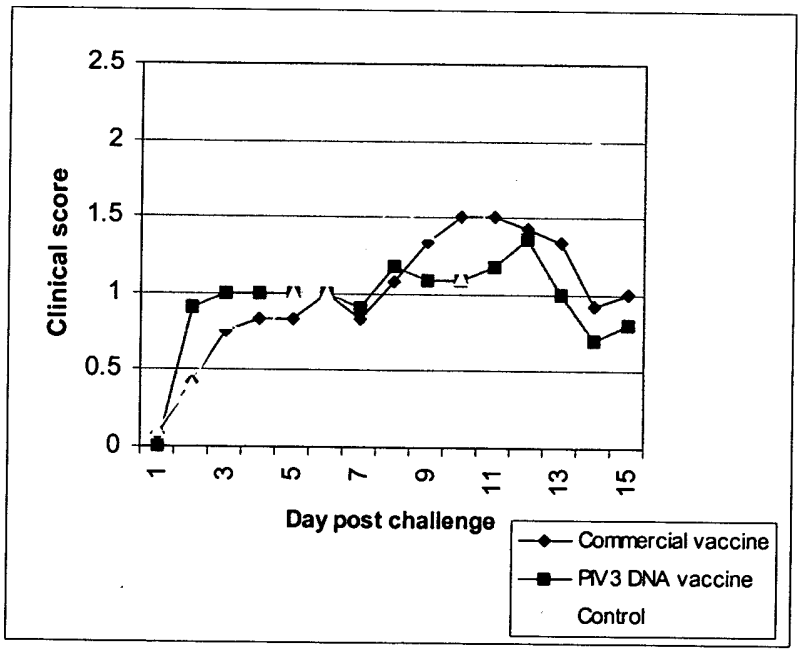


Table 2.

Day	% excreting animals		
	PIV3 DNA vaccine	Commercial vaccine	Control
1	1	1	1
2	1	1	1
3	1	1	1
4	1	0.91	1
5	0.64	0.44	1
6	0.18	0	0.78
7	0	0	0.3

Figure 2.

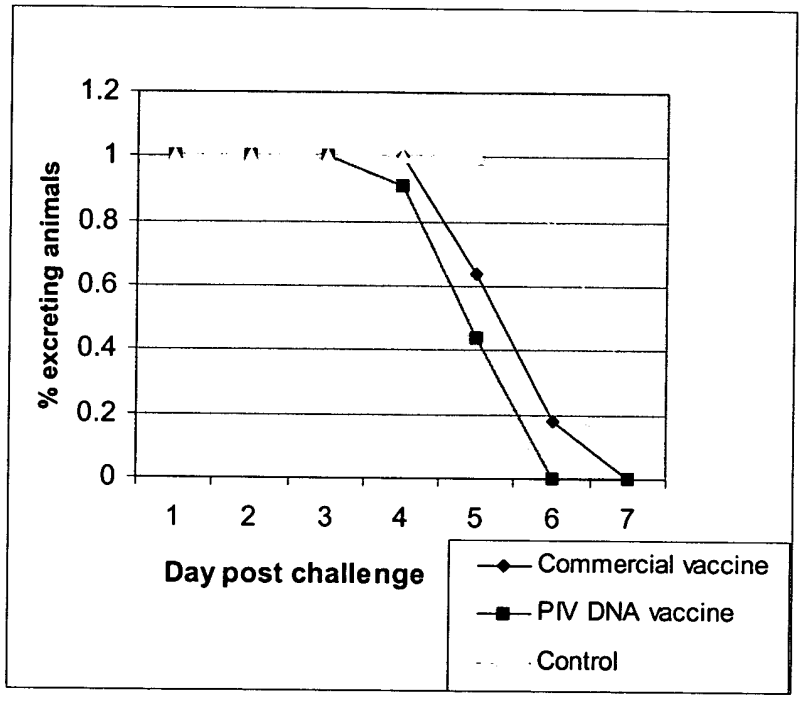


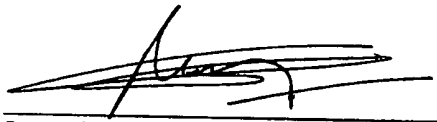
Table 3.

Day	Neutralizing titers		
	PIV3 DNA vaccine	Commercial vaccine	Control
0	0.5	0.5	0.5
56	1.8	1.2	0.5

4. The data presented herein demonstrates that the claimed immunogenic composition is efficacious at reducing the clinical score and viral excretion and at raising neutralizing titers in bovines following viral challenge. This is the first such demonstration with a plasmid vaccine containing and expressing BPIV-3 HN and/or F proteins. Because results cannot be extrapolated from rodents to larger animals, it is submitted that no expectation of success can be found in the references cited in the Office Action or in the prior art at all. Therefore, I believe that the claimed invention is patentable and non-obvious over the cited references. Therefore, reconsideration and withdrawal of the rejections under 35 U.S.C. §103(a) are requested.

5. All statements made herein of my own knowledge are true and all statements made on information and belief are believed to be true. These statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Date: NOVEMBER 3, 2003



Jean-Christophe Audonnet